PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Michael O'REILLY et al.

Art Unit: **Huff, S.**

Serial No.: **To be Assigned**

Examiner: **1642**

Filed: **Herewith**

For: **THERAPEUTIC ANTIANGIOGENIC ENDOSTATIN COMPOSITIONS**

INFORMATION DISCLOSURE STATEMENT
UNDER 37 C.F.R. §§ 1.97 AND 1.98

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

In accordance with the requirements of 37 C.F.R. §§ 1.56, 1.97-1.98 and MPEP § 609, the Applicant, through his attorneys, hereby brings to the attention of the Examiner the references noted on the attached Form PTO-1449.

The Examiner is respectfully requested to initial in the space adjacent to the listing on Form PTO-1449, and return a copy of the initialed Form PTO-1449 with the next communication to Applicant, to confirm that these documents have been considered by the Examiner and made of record in this application.

Since this statement is being filed before the first Office Action has been mailed, no fees are believed to be necessary; however, the Commissioner is hereby authorized to charge any additional fees under 37 C.F.R. 1.16 or 1.17 which may be required during the entire pendency of this application, or to credit any overpayment, to Deposit Account No. 501458.

The above information is presented so that the United States Patent and Trademark Office may, in the first instance, determine any materiality thereof to the claimed invention. See 37 C.F.R. §§ 1.104(a) and 1.106(b) regarding the PTO's duty to consider and use any such information. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited " on any patent to issue therefrom.

Respectfully submitted,

Date: January 11, 2002

By: H. Khalilian

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ATTY. DOCKET NO.	SERIAL NO.	FILING DATE
05213-0229	NOT YET AVAILABLE	Filed Herewith
APPLICANT		GROUP
O'REILLY, ET AL		

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AA						
	AB						
	AC						
	AD						
	AE						
	AF						
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	AH						
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FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	NAME	TRANSLATION YES	TRANSLATION NO.
	AK	WO 95/29242	11/02/95	PCT			
	AL	WO 95/25543	09/28/95	PCT			
	AM	WO 93/16716	09/02/93	PCT			
	AN	WO 91/10424	07/25/91	PCT			
	AO	J58036391	03/03/83	Japan (Abstract)			

OTHER REFERENCES (*Including Author, Title, Date, Pertinent Pages, Etc.*)

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	BA		Abe, N. et al., "Identification of a Novel Collagen Chain Represented by Extensive Interruptions in the Triple-Helical Region", *Biochem. and Biophy. Resch. Comm.*, Vol. 196, No. 2, pp. 576-582 (1993)
	BB		Algire, G.H. et al., "Vascular reactions of normal and malignant tumors in vivo. I. Vascular reactions of mice to wounds and to normal and neoplastic transplants", *J. Natl. Canc. Inst.*, Vol. 6, pp. 73-85 (1945)
	BC		Angiolillo, A.l. et al., "Human interferon-inducible Protein 10 is a potent inhibitor of angiogenesis in vivo", *J. Exp. Med.* ,Vol. 182, pp. 155-162 (1995)
	BD		Brem, H. et al., "Interstitial chemotherapy with drug polymer implants for the treatment of recurrent gliomas", *J. Neurosurg.*, Vol. 74, pp. 441-446 (1991)
	BE		Brockway, W. J. et al., "Measurement of the Binding of Antifibrinolytic Amino Acids to Various Plasminogens", *Arch. Biochem. Biophys.*, Vol. 151, pp. 194-199 (1972)
	BF		Browne, M.J. et al., "Expression of Recombinant Human Plasminogen and Aglycoplasminogen in HeLa Cells", *Fibrinolysis*, Vol. 5, pp. 257-260 (1991)
	BG		Cao, Y. et al., "gro-ß, α -C-X-C- Chemokine, Is an Angiogenesis Inhibitor That Suppresses the Growth of Lewis Lung Carcinoma in Mice", *J. Esp. Med.*, Vol. 182, pp. 2069-2077 (1995)
	BH		Chen, C. et al., "A Strategy to Discover Circulating Angiogenesis Inhibitors Generated by Human Tumors", *Canc Resch.*, Vol. 55, pp. 4230-4233 (1995)
	BI		Clapp, C. et al., "The 16-kilodalton N-terminal fragment of human prolactin is a potent inhibitor of angiogenesis", *Endocrinology* ,Vol. 133, pp. 1292-1299 (1993)
	BJ		Cleary, S. Mulkerrin et al., "Purification and Characterization of Tissue Plasminogen Activator Kringle-2 Domain Expressed in *Escherichia coli*", *Biochem.*, Vol. 28, pp. 1884-1891 (1989)
	BK		Dameron, K.M. et al., "Control of angiogenesis in fibroblasts by p53 regulation of thrombospondin-1", *Science*, Vol. 265, pp. 1582-1584 (1994)
	BL		Folkman, J., "Tumor angiogenesis and tissue factor", *Nature Med.* Vol. 2, pp. 167-168 (1996)
	BM		Folkman, J., "What is the Evidence that Tumors are Angiogenesis Dependent?", *J. Natl Canc Inst.*, Vol. 82, pp. 4-6 (1990)
	BN		Folkman, J., "Angiogenesis in cancer, vascular, rheumatoid and other disease", *Nature Medicine*, Vol. 1, No. 1, pp. 27-31 (1995)
	BO		Folkman, J., "Long-term culture of capillary endothelial cells", *Proc. Natl. Acad. Sci. USA* 76, pp. 5217-5221 (1979)
	BP		Folkman, J. et al., "Induction of angiogenesis during the transition from hyperplasia to neoplasia", *Nature*, Vol. 339, pp. 58-61 (1989)
	BQ		Folkman, J. et al. ,"Tumor Behavior in Isolated Perfused Organs In Vitro Growth and Metastases of Biopsy Material in Rabbit Thyroid and Canine Intestinal Segment", *Annals of Surgery*, Vol. 164, No. 3, pp. 491-501 (1996)
	BR		Folkman, J. , "Angiogenesis and Its Inhibitors", *Important Advances in Oncology*, J.B. Lippincott Company, pp. 42-62 (1985)
	BS		Folkman, J., "Tumor Angiogenesis Therapeutic Implications", *NE J. of Med.*, No. 18, pp. 1182-1186 (1971)

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	CA		Gavrieli, Y. et al., "Identification of programmed cell death in situ via specific labeling of nuclear DNA fragmentation", *J. CellBiol.*, Vol. 119, pp. 493-501 (1992)
	CB		Gimbrone, M.A. et al., "Tumor Growth and Neovascularization An Experimental Model using the Rabbit Cornea", *J. Natl. Canc. Inst.*, Vol. 52, No. 2 pp. 413-427 (1974)
	CC		Gimbrone, M.A. et al., "Tumor Dormancy in Vivo by Prevention of Neovascularization", *J. of Experi. Med.*, Vol. 136, pp. 261-276 (1972)
	CD		Good, D.J. et al., "A tumor suppressor-dependent inhibitor of angiogenesis is immunologically and functionally indistinguishable from a fragment of thrombospondin", *Proc. Nat. Acad. Sci. USA*, Vol. 87, pp. 6624-6628 (1990)
	CE		Grant, D.S. et al., "Scatter factor induces blood vessel formation in vivo", *Proc. Natl. Acad. Sci. USA*, Vol. 99, pp. 1937-1941 (1993)
	CF		Grant, D.S. et al., "Two different laminin domains mediate the differentiation of human endothelial cells into capillary-like structures in vitro", *Cell*, Vol. 58, pp. 933-943 (1989)
	CG		Gross, J.L. et al., "Modulation of Solid Tumor Growth in vivo by bFGF", *Proc. Amer. Assoc. Canc. Resh*, Vol. 31, p. 79 (1990)
	CH		Gross, J.L. et al., "Increased capillary endothelial cell protease activity in response to angiogenic stimuli in vitro.", *Proc. Natl. Acad. Sci. USA*, Vol. 80, pp. 2623-2627 (1983)
	CI		Gunzler, W.A. et al., "The Primary Structure of High Molecular Mass Urokinase from Human Urine", *Hoppe-Seyler's Z. Physiol. Chem.*, Vol. 363, pp. 1155-1165 (1982)
	CJ		Gupta, S.K. et al., "A potent inhibitor of endothelial cell proliferation is generated by proteolytic cleavage of the chemokine platelet factor 4", *Proc. Natl. Acad. Sci. USA*, Vol. 92, pp. 7779-7803 (1995)
	CK		Holmgren, L. et al., "Dormancy of micrometastases Balanced proliferation and apoptosis in the presence of angiogenesis suppression", *Nature Medicine*, Vol. 1, No. 2, pp. 149-153 (1995)
	CL		Homandberg, G.A. et al., "Heparin-binding fragments of fibronectin are potent inhibitors of endothelial cell growth", *Am. J. Path.*, Vol. 120, pp. 327-332 (1985)
	CM		Hori, A. et al., "Suppression of Solid tumor Growth by Immunoneutralizing Monoclonal Antibody against Human Basic Fibroblast Growth Factor", *Canc. Resch.*, Vol. 51, pp. 6180-6184 (1991)
	CN		Ingber, D. et al., "Synthetic analogues of fumagillin that inhibit angiogenesis and suppress tumor growth", *Nature*, Vol. 348, pp. 555-557 (1990)
	CO		Johansson, J. et al., "Surfactant Protein B: Disulfide Bridges, Structural Properties, and Kringle Similarities", *Biochem.*, Vol. 30, pp. 6917-6921 (1991)
	CP		Kandel, J. et al., "Neovascularization is Associated with a Switch to the Export of bFGF in the Multistep Development of Fibrosarcoma", *Cell*, Vol. 66, pp. 1095-1104 (1991)
	CQ		Kim, K. J. et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumor growth in vivo", *Nature*, Vol. 362, pp. 841-844 (1993)
	CR		Kivirikko, S. et al., "Primary Structure of the α1 Chain of Human Type XV Collagen and Exon-Intron Organization in the 3' Region of the Corresponding Gene", *J. Bio. Chem.*, Vol. 269, No. 7, pp. 4773-4779 (1994)

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	DA		Knighton, D. et al., "Avascular and Vascular Phases of Tumor Growth in the Chick Embryo", *Br. J. Cancer*, Vol. 35, pp. 347-356 (1977)
	DB		Lein, W. M. et al., "The blood supply of experimental liver metastases. II. A Microcirculatory study of the normal and tumor vessels of the liver with the use of perfused silicone rubber", *Surgery*, Vol. 68, No. 2, pp. 334-340 (1970)
	DC		Lerch et al., "Localization of Individual Lysine-Binding Regions in Human Plasminogen and Investigations on Their Complex-Forming Properties", *European Journal of Biochemistry*, Vol. 107, No. 1, pp. 7-13 (1980)
	DD		Lokker, N.A. et al., "Mutational analysis and molecular modeling of the N-terminal kringle-containing domain of hepatocyte growth gactor identifies amino acid side chains important for interaction with the c-met receptor", *Prot. Engin.*, Vol. 7, pp. 895-903 (1994)
	DE		Maione, T.E. et al., "Inhibition of Angiogenesis by Recombinant Human Platelet Factor-4 and Related Peptiddes", *Science*, Vol. 247, pp. 77-79 (1990)
	DF		Marti, D. et al., "Expression, purification and characterization of the recombinant kringle 2 and kringle 3 domains of human plasminogen and analysis of their binding affinity for ω-aminocarboxylic acids", *Eur. J. Biochem.*, Vol. 219, pp. 455-462 (1994)
	DG		McLean, J.W. et al., "cDNA sequence of human apolipoprotein(a) is homologous to plasminogen", *Nature*, Vol. 330, pp. 132-137 (1987)
	DH		Menhart, N. et al., "Construction, Expression, and Purification of Recombinant Kringle 1 of Human Plasminogen and Analysis of Its Interaction with ω–Amino Acids", *Biochem.*, Vol. 30, pp. 1948-1957 (1991)
	DI		Millauer, B. et al., "Glioblastoma growth inhibited in vivo by a dominant-negative Flk-1 mutant", *Nature*, Vol. 367, pp. 576-579 (1994)
	DJ		Moses, M.A. et al., "Identification of an Inhibitor of Neovascularization from Cartilage", *Science*, Vol. 248 (1990)
	DK		Muragaki, Y. et al., "Mouse col 18a1 is expressed in a tissue-specific manner as three alternative variants and is localized in basement membrane zones", *Proc. Natl. Acad. Sci.* USA, Vol. 92, pp. 8763-8767 (1995)
	DL		Muthukkaruppan, VR., "Angiogenesis in the Mouse Cornea", *Science*, Vol. 205, pp. 1416-1418 (1979)
	DM		Nelson, J. A. et al., "Murine epidermal growth factor (EGF) fragment (33-42) inhibits both EGF- and laminin-dependent endothelial cell motility and angiogenesis", *Canc. Resch.*, Vol. 55, pp. 3772-3776 (1995)
	DN		Nguyen, M. et al., "Quantitation of Angiogenesis and Antiangiogenesis in the Chick Embryo Chorioallantoic Membrane", *Microvascular Research*, Vol. 47, pp. 31-49 (1994)
	DO		Nguyen, M. et al., "Elevated Levels of the Angiogenic Peptide Basic Fibroblast Growth Factor in Urine of Bladder Cancer Patients", *J. of Nat. Canc. Inst.*, Vol. 85, No. 3, pp. 241-242 (1993)
	DP		O'Reilly et al., "Endogenous Inhibitors of Angiogenesis", *Proc. Am. Assoc. Canc. Resch.*, Vol. 37, p. 669 (1996)
	DQ		O'Reilly et al., "Angiostatin induces and sustains dormancy of human primary tumors in mice", *Nature Medicine*, Vol. 2, No. 6, pp. 689-692 (1996)
	DR		O'Reilly et al., "The suppression of Tumor Metastases by a Primary Tumor", *Surgical Forum*, Vol. XLIV, pp. 474-476 (1993)
	DS		O'Reilly et al., "Angiostatin A Novel Angiogenesis Inhibitor that Mediates the Suppression of Metastases by a Lewis Lung Carcinoma", *Cell*, Vol. 79, pp. 315-328 (1994)
	DT		O'Reilly et al., "Angiostatin: A Circulating Endothelial Cell Inhibitor That Suppresses Angiogenesis and Tumor Growth", *Cold Spring Harbor Symposia on Quantitative Biology*, Vol. LIX, pp. 471-482 (1994)
	DU		Obeso, J. et al., "Methods in Laboratory Investigation/A Hemangioendothelioma-Derived Cell Line Its Use as a Model for the Study of Endothelial Cell Biology", *Laboratory Investigation*, Vol. 63, No. 2, p. 159 (1990)
	DV		Oh, S.K. et al., "Isolation and sequencing of cDNAs for proteins with multiple domains of Gly-Xaa-Yaa repeats identify a distinct family of collagenous proteins", *Proc. Natl. Acad. Sci.* USA, Vol. 91, pp. 4229-4233 (1994)

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	EA		Oh, S.P., "Cloning of cDNA and Genomic DNA Encoding Human Type VIII Collagen and Localization of the α1(XVIII) Collagen Gene to Mouse Chromosome 10 and Human Chromosome 21", *Genomics*, Vol. 19, pp. 494-499 (1994)
	EB		Parangi, S. et al, "Antiangiogenic therapy of transgenic mice impairs de novo tumor growth", *Proc. Natl. Acad. Sci. USA*, Vol. 93, pp. 2002-2007 (1996)
	EC		Passaniti, A. et al., "Methods in Laboratory Investigation/A Simple, Quantitative Method for Assessing Angiogenesis and Antiangiogenic Agents Using Reconstituted Basement Membrane, Heparin, and Fibroblast Growth Factor", *Lab. Invest.*, Vol. 67, No. 4, pp. 519-528 (1992)
	ED		Ponting et al., "Plasminogen: a structural review", *Blood Coagulation and Fibrinolysis*, Vol. 3, pp. 605-614 (1992)
	EE		Powell, J. R. et al., "Amino Acid Sequence Analysis of the Asparagine-288 Region of the Carbohydrate Variants of Human Plasminogen", *Biochem,*. Vol. 22, pp. 923-927 (1983)
	EF		Rastinejad, F. et al., "Regulation of the activity of a new inhibitor of angiogenesis by a cancer suppressor gene", *Cell*, Vol. 56, pp. 345-355 (1989)
	EG		Rehn, M. et al., "α1(XVIII), a collagen chain with frequent interruptions in the collagenous sequence, a distinct tissue distribution, and homology with type XV collagen", *Proc. Natl. Acad. Sci. USA*, Vol. 91, pp. 4234-4238 (1994)
	EH		Rehn, M. et al., "Identification of three N-terminal ends of type XVIII collagen chains and tissue-specific differences in the expression of the corresponding transcripts", *J. Biol. Chem.*, Vol. 270, pp. 5705-4711 (1995)
	EI		Robbins, K.C., "The Plasminogen-Plasmin Enzyme System", *Fibrinolysis*, pp. 340-357 (1987)
	EJ		Sage, E.H. et al., "Inhibition of Endothelial Cell Proliferation by SPARC is Mediated through a Ca^{2+}-Binding EF-Hand Sequence", *J. Cell. Biochem.*, Vol. 57, pp. 127-140 (1995)
	EK		Sakamato, N. et al., "Inhibition of angiogenesis and tumor growth by a synthetic laminin peptide, CDPGYIGSR-NH_2" *Canc. Resch.*, Vol. 51, pp. 903-906 (1991)
	EL		Sambrook, J. et al., "Expression of Cloned Genes in Escherichia coli", *Molecular Cloning Second Edition*, Cold Spring Harbor Laboratories Press, pp. 17.37-17.41
	EM		Schaller, J. et al., "Structural Aspects of the Plasminogen of Various Species", *Enzyme*, 40 pp. 63-69 (1988)
	EN		Shi, G. et al., "Kringle Domains and Plasmin Denaturation", *Biochem. Biophy. Resch. Comm.*, Vol. 178, No. 1, pp. 360-368 (1991)
	EO		Sottrup-Jensen, L. et al., "The Primary Structure of Human Plasminogen Isolation of Two Lysine-Binding Fragments and One "Mini-" Plasminogen (MW, 38,000) by Elastase-Catalyzed-Specific Limited Proteolysis", *Prog. in Chem. Fibrinolysis and Thrombolysis*, Vol. 3, pp. 191-209 (1978)
	EP		Srivastava, A. et al., "The Prognostic Significance of Tumorascularity in Intermediate-Thickness (0.76-4.0mm Thick) Skin Melanoma", *Am. J. of Path.*, Vol. 133, No. 2. , pp. 419-424 (1988)
	EQ		Strieter, R.M. et al., "Interferonγ-inducible protein 10 (IP-10), a member of the C-X-C chemokine family, is an inhibitor of angiogenesis. *Biochem. Biophys. Resch. Comm.*, Vol. 210, pp. 51-57 (1995)
	ER		Studier, W.F. et al., "Use of T7 RNA polymerase to direct expression of cloned genes", *Methods Enzymol.*, Vol. 85, pp. 60-89 (1990)
	ES		Teicher, B.A. et al., "Potentiation of cytotoxic cancer therapies by TNP-470 alone and with other antiangiogenic agents", *Int. J. Canc.*, Vol. 57, pp. 1-6 (1994)
	ET		Tolsma, S.S. et al., "Peptides derived from two separate domains of the matrix protein thrombospondin-1 have antiangiogenic activity", *J. Cell Biol.*, Vol. 122, pp. 497-511 (1993)
	EU		Van Meir, E. et al., "Release of an inhibitor of angiogenesis upon induction of wild type p53 expression in glioblastoma cells", *Nature Genetics*, Vol. 8, pp. 171-176 (1994)
	EV		Voest, E. E. et al., "Inhibition of Angiogenesis in Vivo by Interleukin 12", *J. Natl. Can. Inst.*, Vol. 87, pp. 581-586 (1995)

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	FA		Walz, D.A. et al., "Amino acid sequence of human prothrombin fragments 1 and 2", *Proc. Natl. Acad. Sci.*, Vol. 74, pp. 1969-1973 (1977)
	FB		Weidner, N. et al., "Tumor Angiogenesis: A New Significant and Independent Prognostic Indicator in Early-Stage Breast Carcinoma", *J. Natl. Canc. Inst.*, Vol. 84, pp. 1875-1887 (1992)
	FC		Weidner, N. et al., "Tumor Angiogenesis Correlates with Metastasis in Invasive Prostate Carcinoma", *Am. J. Path.*, Vol. 143, No. 2, pp. 401-409 (1993)
	FD		Weidner, N. et al., "Tumor Angiogenesis and Metastasis - Correlation in Invasive Breast Carcinoma", *NE J. of Med.*, Vol. 324, No. 1, pp. 1-8 (1991)
	FE		Wiman, B. et al., "On the Specific Interaction Between the Lysine-Binding Sites in Plasmin and Complementary Sites In α_2-Antiplasmin and Fibrinogen", *Biochimica et Biophysica Acta*. Vol. 579, pp. 142-154 (1979)
	FF		Yoshimura, T. et al., "Cloning, Sequencing, and Expression of Human Macrophage Stimulating Protein (MSP, MST1) Confirms MSP as a Member of the Family of Kringle Proteins and Locates the MSP Gene on Chromosome 3", *Laboratory of Immunobiology*, pp. 15461-15468 (1993)
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Sheet 1 of 2

Complete if Known	
Application Number	09/315,689
Filing Date	May 20, 1999
First Named Inventor	M. Judah Folkman
Group Art Unit	1642
Examiner Name	S. Huff
Attorney Docket Number	05213-0229 (43170-219534)

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	U.S. Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

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Examiner Initials	Cite No.[1]	Foreign Patent Document Office[3]	Number[4]	Kind Code[5] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	1	CN	1 177 005 A		Xu Genxing	03-25-1998	Abstract	
	2	WO	97 15666 A		Children's Medical Center	05-01-1997	Page 1. line 23- line 32	

Examiner Signature		Date Considered	

[1]Unique citation designation number. [2]See attached Kinds of U.S. Patent Documents. [3]Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4]For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5]Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6]Applicant is to place a check mark here if English language translation is attached.

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Sheet 2 of 2

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Examiner Name	S. Huff
Attorney Docket Number	05213-0229 (43170-219534)

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	3	Blezinger, Paul, et al. "Systemic Inhibition of tumor growth and tumor metastases by intramuscular administration of the Endostatin gene" NATURE BIOTECHNOLOGY, vol.17, April 1999, pp 343-348.	
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Examiner Signature		Date Considered	

[1]Unique citation designation number. [2]Applicant is to place a check mark here if English language translation is attached.